

In re Application of: Schiffer & Heinemann
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PATENT
Attorney Docket No.: SALK2940
(088802-8051)

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APPENDIX A

PENDING CLAIMS FOR SALK2940 (088802-8051)

1. A method of determining predisposition of a subject to a mood disorder, said method comprising determining in a biological sample of a subject, the presence of a kainate receptor subunit GluR7 allelic genotype or allelic phenotype associated with predisposition to a mood disorder.
2. The method of claim 1, wherein said allelic genotype is homozygosity for a thymine containing nucleotide at position 928 (928T/T) or homozygosity for a guanine containing nucleotide position 928 (928G/G).
3. The method of claim 2, wherein said 928T/T homozygosity is associated with recurrent unipolar depressive disorder.
4. The method of claim 2, wherein said 928 G/G homozygosity is associated with bipolar II depressive disorder.
5. The method of claim 1, wherein said allelic phenotype is homozygosity for a serine at amino acid position 310 (310 Ser/Ser) or homozygosity for an alanine at position 310 (310 Ala/Ala).
6. The method of claim 5, wherein said 310Ser/Ser homozygosity is associated with recurrent unipolar depressive disorder.
7. The method of claim 5, wherein said 310Ala/Ala homozygosity is associated with bipolar II depressive disorder.

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8. A method of determining predisposition to a mood disorder in a subject having a T/G heterozygosity at nucleotide position 928 in the GluR7 gene, said method comprising determining in a biological sample of the subject, a predominance in the expression of either the T allele or the G allele.
9. The method of claim 8, wherein said predominance of expression of the T allele is associated with predisposition to recurrent unipolar depressive disorder.
10. The method of claim 8, wherein said predominance of expression of the G allele is associated with predisposition to bipolar II depressive disorder.
11. The method of claim 8 where said predominance of expression is about 1.2 fold or greater.
12. The method of claim 8, wherein said predominance is determined by comparing the level of expression of said T and G alleles in GluR7 mRNA.
13. The method of claim 8, wherein said predominance is determined by comparing the level of expression of GluR7 protein., wherein said T allele results in a GluR7 protein having serine at position 310 and said G allele results in a GluR7 protein having an alanine at position 310.
14. A kit for determining predisposition of a subject to a mood disorder, said kit comprising at least one reagent specific for detecting a kainate receptor subunit GluR7 allele associated with a mood disorder.
15. The kit of claim 14, wherein said specific reagent is an oligonucleotide.
16. The kit of claim 14, wherein said specific reagent is an antibody

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17. The kit of claim 15, wherein said oligonucleotide hybridizes specifically to the human GluR7 gene or mRNA when the nucleotide at position 928 is a thymine.
18. The kit of claim 15, wherein said oligonucleotide hybridizes specifically to the human GluR7 gene or mRNA when the nucleotide at position 928 is a guanine.
19. The kit of claim 15, wherein said oligonucleotide hybridizes specifically to the human GluR7 gene or mRNA when the nucleotide at position 928 is a thymine.
20. The kit of claim 16, wherein said antibody binds specifically to the human GluR7 protein when the amino acid at position 310 is an alanine.
21. The kit of claim 16, wherein said antibody binds specifically to the human GluR7 protein when the amino acid at position 310 is a serine.
22. A method of treating or preventing a mood disorder effected by abnormal GluR7 receptor subunit activity or function in a subject, said method comprising administering to said subject an effective amount of a compound that modulates GluR7 receptor subunit activity or function.
23. The method of claim 22, wherein said compound modifies the activity or function of the GluR7 receptor subunit having a thymine at nucleotide position 928 of the human GluR7 receptor subunit.
24. The method of claim 22, wherein said individual is homozygous for the human GluR7 allele having a thymine at nucleotide position 928.
25. The method of claim 22, wherein said compound modifies the activity or function of the GluR7 receptor subunit having a guanine at nucleotide position 928 of the human GluR7 receptor subunit.
26. The method of claim 22, wherein said individual is homozygous for the human GluR7 allele having a thymine at nucleotide position 928.
27. The method of claim 23, wherein said mood disorder is recurrent unipolar depressive disorder.

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28. The method of claim 25, wherein said mood disorder bipolar II depressive disorder.
29. The method of claim 22, wherein said compound is identified by
- a) incubating a cell expressing a GluR7 receptor subunit with the compound under conditions sufficient to permit the compound to interact with cell; and
 - b) comparing the activity or function of said GluR7 receptor subunit incubated in the presence of the compound with the activity or function of a GluR7 receptor subunit in the absence of the compound, thereby identifying a compound that modulates GluR7 receptor subunit activity or function.
30. The method of claim 29, wherein said compound is selected from the group consisting of peptides, peptidomimetics, polypeptides, pharmaceuticals, biological agents, antibodies, neurotropic agents, and combinatorial compound libraries.
31. The method of claim 29, wherein said cell is a neuronal cell or a glial cell.
32. A transgenic non-human animal as a model of a human mood disorder, said transgenic animal having a genome comprising a disruption of the endogenous GluR7 genes and insertion of a functional human GluR7 gene.
33. The transgenic animal of claim 32, wherein said GluR7 gene has a thymine at nucleotide position 928.
34. The transgenic animal of claim 32, wherein said GluR7 gene has a guanine nucleotide position 928.
35. The transgenic animal of claim 32, wherein said disruption comprises the insertion of a transgene comprising a selectable marker sequence.
36. The transgenic animal of claim 32, wherein said animal is murine.